REMARKS

I. Status Summary

Claims 1, 7, 8, 12 and 13 are pending in the subject application. Claims 7, 8 and 12 have been withdrawn pursuant to a Restriction/Election Requirement issued by the U.S. Patent and Trademark Office (hereinafter "the Patent Office"). Claims 1 and 13 presently stand rejected.

Claim 1 presently stands rejected under the provisions of 35 U.S.C. § 102(b) as allegedly being anticipated by Ishikawa et al. (1997, *DNA Research* 4(5):307-313; hereinafter "Ishikawa et al."), as evidenced by GenBank Accession No. BAA23691.2.

Claims 1 and 13 have been rejected under 35 U.S.C. §103(a) upon the contention that the claims are unpatentable over PCT International Patent Application Publication No. WO 01/57190 to Tang et al. (hereinafter referred to as "Tang et al.") in view of GenBank Accession No. BAA23691.2.

Claim 1 has been amended. Support for the amendments can be found throughout the specification as originally filed, and in particular at page 23, line 31, through page 24, line 1; and in Figure 14. No new matter has been added.

Reconsideration of the application based on the amendments and arguments set forth herein is respectfully requested.

II. Response to the 35 U.S.C. § 102(b) Rejection of Claim 1

Claim 1 has been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ishikawa et al. as evidenced by GenBank Accession No. BAA23691.2. The Patent Office contends that Ishikawa et al. teach a protein of 459 amino acids encoded by cDNA clone KIAA0395. Further, the Patent Office contends that GenBank Accession No. BAA23691.2 shows the amino acid sequence of the KIAA0395 protein taught by Ishikawa et al. The Patent Office contends that the sequence of KIAA0395 is 100% identical to amino acids 242-502 of SEQ ID NO: 1 and is more than 85% identical to SEQ ID NO: 1. As such, the Patent Office contends that the high percent identity indicates that the KIAA0395 protein would

have the same function as instant SEQ ID NO: 1. Thus, the Patent Office asserts that Ishikawa et al. teaches each and every element of the rejected claims such that the claims are anticipated.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Applicants preliminarily note it is well settled that for a cited reference to qualify as prior art under 35 U.S.C. §102, each element of the claimed subject matter must be disclosed within the reference. "A claim is anticipated only if each and every element in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Claim 1 is directed to a drug agent to repress transcription of a type II hexokinase or a pyruvate kinase M gene expressed specifically in hepatoma cells. Applicants respectfully submit that Ishikawa et al. fails to disclose a drug agent as presently claimed. Ishikawa et al. also fails to disclose the transcriptional repressor activity of the protein encoded by SEQ ID NO: 1, as taught and claimed in the instant application. Ishikawa et al. fails to disclose a protein having transcriptional repressor activity in the context of a drug agent as presently claimed. Ishikawa et al. specifically fails to disclose the transcriptional repression of the expression of type II hexokinase or pyruvate kinase M genes. Therefore, the disclosure of Ishikawa et al. fails to teach each and every element claim 1.

Notwithstanding the above and without acquiescing to the contentions of the Patent Office, applicants respectfully submit that claim 1 has been amended to more clearly recite the claimed subject matter. In particular, applicants respectfully submit that claim 1 has been amended to recite, a drug agent to repress transcription of a gene expressed specifically in hepatoma cells, comprising a protein as an effective component having an amino acid sequence of SEQ ID NO: 1, wherein the protein comprises amino acids 1-107 and 242-555 of SEQ ID NO: 1 and has at least 85%

sequence identity to SEQ ID NO: 1, wherein the gene is a type II hexokinase or a pyruvate kinase M gene. Support for the amendments can be found throughout the specification as originally filed, and in particular at page 23, line 31, through page 24, line 1; and in Figure 14. No new matter has been added.

Applicants respectfully submit that Ishikawa et al. does not teach a drug agent to repress transcription of a gene expressed specifically in hepatoma cells, comprising a protein as an effective component having an amino acid sequence of SEQ ID NO: 1, wherein the protein comprises amino acids 1-107 and 242-555 of SEQ ID NO: 1 and has at least 85% sequence identity to SEQ ID NO: 1, wherein the gene is a type II hexokinase or a pyruvate kinase M gene, as presently recited in claim 1.

Accordingly, applicants respectfully submit that Ishikawa et al. does not support a rejection of claim 1 under 35 U.S.C. § 102(b). Thus, withdrawal of the instant rejection of claim 1 under 35 U.S.C. § 102(b) is respectfully requested. A Notice of Allowance is also respectfully requested.

III. Response to the 35 U.S.C. § 103(a) Rejection of Claims 1 and 13

Claims 1 and 13 have been rejected under 35 U.S.C. §103(a) upon the contention that the claims are unpatentable over Tang et al. in view of GenBank Accession No. BAA23691.2. Particularly, the Patent Office asserts that Tang et al. teaches an amino acid sequence (SEQ ID NO: 1479) that is 99.9% identical to the amino acid sequence of SEQ ID NO: 1. The Patent Office contends that it would have been within the skill of one of ordinary skill in the art to make a single amino acid substitution in the sequence of Tang et al. based upon a sequence comparison with the homologous peptide disclosed in GenBank Accession No. BAA23691.2 to arrive at the presently claimed subject matter.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Initially, applicants respectfully submit that claim 1 has been amended to more clearly recite the claimed subject matter. In particular, applicants respectfully submit that claim 1 has been amended to recite, a drug agent to repress transcription of a gene expressed specifically in hepatoma cells, comprising a protein as an effective component having an amino acid sequence of SEQ ID NO: 1, wherein the protein comprises amino acids 1-107 and 242-555 of SEQ ID NO: 1 and has at least 85% sequence identity to SEQ ID NO: 1, wherein the gene is a type II hexokinase or a pyruvate kinase M gene. Support for the amendments can be found throughout the specification as originally filed, and in particular at page 23, line 31, through page 24, line 1; and in Figure 14. No new matter has been added.

Applicants respectfully submit that Tang et al., alone or in view of GenBank Accession No. BAA23691.2, does not teach or suggest a drug agent to repress transcription of a gene expressed specifically in hepatoma cells, comprising a protein as an effective component having an amino acid sequence of SEQ ID NO: 1, wherein the protein comprises amino acids 1-107 and 242-555 of SEQ ID NO: 1 and has at least 85% sequence identity to SEQ ID NO: 1, wherein the gene is a type II hexokinase or a pyruvate kinase M gene, as presently recited in present claim 1. Likewise, applicants respectfully submit that Tang et al., alone or in view of GenBank Accession No. BAA23691.2, does not teach or suggest a drug agent to repress transcription of a gene expressed specifically in hepatoma cells, comprising a protein consisting of amino acid sequence SEQ ID NO: 1 as an effective component, wherein the gene is a type II hexokinase or a pyruvate kinase M gene, as recited in claim 13. Accordingly, applicants respectfully submit that claims 1 and 13 are believed to be patentable over Tang et al. in view of GenBank Accession No. BAA23691.2.

To elaborate, the Patent Office contends that it would have been within the skill of the art at the time the invention was made for the ordinary artisan to align the sequence of Tang et al. (SEQ ID NO: 1479) with the sequence of GenBank Accession No. BAA23691.2. The Patent Office then contends that it would have

been within the skill of one of ordinary skill in the art to make a single amino acid substitution, i.e. change the asparagine residue at position 310 of SEQ ID NO: 1479 to a serine residue, based upon the sequence comparison. In particular, the Patent Office asserts that because GenBank Accession No. BAA23691.2 teaches a homologous peptide with a serine at position 310, it would have been within the skill of the art at the time of the invention to replace the asparagine at position 310 of SEQ ID NO: 1479 with a serine in order to achieve the predictable result of providing a functional protein by substituting one naturally occurring amino acid for another. Applicants respectfully disagree.

Applicants respectfully direct the Patent Office to part III of section 2143.01 of the MPEP, which recites:

> The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *KSR*, 550 U.S. 398, 82 USPQ2d 1385, 1396.

Likewise, part IV of this section of the MPEP also states:

> A statement that modifications of the prior art to meet the claimed invention would have been "'well within the ordinary skill of the art at the time the claimed invention was made'" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR*, 550 U.S. 398, 82 USPQ2d 1396 quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Applicants respectfully submit that the Patent Office has made no more than a conclusory assertion that the cited references can be combined without articulating a reason with some rational underpinning to support the legal conclusion of obviousness. This is clearly proscribed by the above-noted sections of the MPEP.

To elaborate, applicants respectfully submit that the Patent Office has failed to articulate why one of ordinary skill in the art would be motivated to select SEQ ID NO: 1479 of Tang et al. from the 3,960 sequences disclosed in Tang et al., and then to align it with GenBank Accession No. BAA23691.2, and then to replace the asparagine at position 310 of SEQ ID NO: 1479 with a serine. The Patent Office appears to contend that this would have been obvious to do in order to achieve the predictable result of providing a functional protein. However, applicants respectfully submit that nowhere does Tang et al. suggest that the protein of SEQ ID NO: 1479 is non-functional, or that the asparagine residue at position 310 should be changed.

Even assuming *arguendo* that one of ordinary skill in the art would be motivated to select SEQ ID NO: 1479 of Tang et al. and to align it with GenBank Accession No. BAA23691.2, neither reference provides motivation for why the residue at position 310 should be changed. Indeed, neither reference teaches or suggests that the functional domain of SEQ ID NO: 1 for suppression of a type II hexokinase or a pyruvate kinase M gene comprises amino acids 242-502. Thus, the Patent Office's contention that the proposed modification of Tang et al. would be obvious to do in order to achieve the predictable result of providing a functional protein appears to be unfounded. Without knowledge of the above-mentioned functional domain of SEQ ID NO: 1 the proposed modification of Tang et al. would not have been apparent to one of ordinary skill in the art, nor would the outcome have been predictable.

Applicants respectfully submit that only after having reviewed the instant specification would one of ordinary skill in the art be motivated to modify Tang et al. as proposed. In particular, only after being armed with the knowledge that amino acids 242-502 comprise a functional domain of SEQ ID NO: 1 and impart the type II hexokinase and pyruvate kinase M gene suppression activity would one of ordinary skill in the art appreciate the potential desirability of modifying SEQ ID NO: 1479 of Tang et al. However, as noted above, Tang et al. does not convey such knowledge. Nor does GenBank Accession No. BAA23691.2. Thus, because neither of the cited

references appear to teach or suggest this aspect of the presently disclosed subject matter, applicants respectfully submit that the Patent Office appears to be improperly relying upon the teachings of the instant disclosure itself as motivation to combine the cited references as proposed. Part X of section 2145 of the MPEP clearly proscribes such hindsight reconstruction, defined as that which includes knowledge gleaned only from applicant's disclosure and which was not within the level of ordinary skill in the art at the time the claimed subject matter was made.

Accordingly, because the Patent Office appears to be improperly relying upon hindsight reconstruction and because the proposed modification of Tang et al. would only be apparent and predictable in view of the teachings in the instant specification, applicants respectfully submit that the Patent Office has failed to establish a *prima facie* case of obviousness. Thus, applicants respectfully request that the instant rejection of claims 1 and 13 under 35 U.S.C. §103(a) upon the contention that the claims are unpatentable over Tang et al. in view of GenBank Accession No. BAA23691.2 be withdrawn. A Notice of Allowance is also respectfully requested.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any additional fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR, & HUNT, P.A.

Date: 09/02/2009 By: _____

Arles A. Taylor, Jr.
Registration No. 39,395
Customer No. 25297
(919) 493-8000

1680/7 AAT/LRL/dbp